

WHAT IS CLAIMED IS:

1. A method for determining a subject's susceptibility to developing a disease or condition, which is caused by or contributed to by an inappropriately high level of IL-1 $\beta$ , comprising the steps of detecting an IL-1B allele (+6912) or an allele in linkage disequilibrium with an IL-1B allele (+6912) in a nucleic acid from the subject, wherein detection of IL-1B allele 2 (+6912) or an allele in linkage disequilibrium with IL-1B allele 2 (+6912) indicates that the patient has an increased susceptibility for developing a disease or condition, which is caused by or contributed to by an inappropriately high level of IL-1 $\beta$ .

2. A method of claim 1, wherein the disease or disorder is an inflammatory disease.

3. A method of claim 2, wherein said inflammatory disorder is selected from the group consisting of: coronary artery disease, osteoporosis, nephropathy in diabetes mellitus, alopecia areata, Graves disease, systemic lupus erythematosus, lichen sclerosis, ulcerative colitis, diabetic retinopathy, periodontal disease, juvenile chronic arthritis (e.g. chronic iridocyclitis), psoriasis, insulin dependent diabetes in DR 3/4 patients, asthma, chronic inflammatory liver disease, chronic inflammatory lung disease, lung fibrosis, liver fibrosis, rheumatoid arthritis and ulcerative colitis.

4. A method of claim 1, wherein the IL-1B allele (+6912) is detected by hybridizing the nucleic acid sample with at least one detection oligonucleotide that contains 6 consecutive nucleotides selected from the group consisting of: 5' ATTAAC 3'; 5' TTAACA 3'; 5' TAACAC 3'; 5' AACACT 3'; 5' ACACTG 3'; 5' CACTGA 3'; 5' ATTAAG 3'; 5' TTAAGA 3'; 5' TAAGAC 3'; 5' AAGACT 3'; 5' AGACTG 3'; and 5' GACTGA 3'.

5. A method of claim 1, wherein the IL-1B allele (+6912) is detected by contacting the sample DNA with a *Hinf*I restriction enzyme and analyzing the restriction fragments, wherein a band pattern of 89, 76 and 61 base pair fragments identifies the IL-1B allele 2 and 76, 61, 54 and 35 bands identify the IL-1B allele 1.

6. A kit for determining a subject's susceptibility to developing a disease or condition, which is caused by or contributed to by an inappropriately high level of IL-1 $\beta$ , said kit comprising a first primer oligonucleotide that hybridizes 5' or 3' to an IL-1B +6912 allele or a marker that is in linkage disequilibrium with an IL-1B +6912 allele.

7. A kit of claim 6, which additionally comprises a second primer oligonucleotide that hybridizes 3' to an IL-1B +6912 marker when the first primer hybridizes 5' and hybridizes 5' to an IL-1B +6912 marker when the first primer hybridizes 3'.

8. A kit of claim 6, wherein said first primer and said second primer hybridize to a region of an IL-1B gene that includes position +6912, wherein said region is in the range of between about 50 and 1000 base pairs.

9. A kit of claim 6 or 7, wherein said primers are selected from the group consisting of:

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- a) 5'GCTCCCACATTCTGATGAGCAAC3'(SEQ. ID. NO. 2);
  - b) 5'TGCAGCACTCAGCAATGAGGAG3'(SEQ. ID. NO. 3);
  - c) 5'CCCATTTAAATCTGAGCTTATATATTTTGAGT3' (SEQ. ID. NO. 4);
  - d) 5'TCAATTTGGACTGGTGTGCTC3' (SEQ. ID. NO. 5); and
  - e) 5'TCAGAACCAATTGAACAGTATGATATTTG3' (SEQ. ID. NO. 6)

10. A kit of claim 9, further comprising a detection means, wherein said detection means is an appropriate amount of *HinfI* restriction enzyme to digest the sample and a means to analyse the digested sample, wherein a band pattern of 89, 76 and 61 base pairs identifies the IL-1B allele 2 and a band pattern of 76, 61, 54 and 35 identify the IL-1B allele 1.

11. A kit of claim 9, further comprising a detection means, wherein said detection means is a detection oligonucleotide that contains 6 consecutive nucleotides selected from the group consisting of: 5' ATTAAC 3'; 5' TTAACA 3'; 5' TAACAC 3'; 5' AACACT 3'; 5' ACACTG 3'; 5' CACTGA 3'; 5' ATTAAG 3'; 5' TTAAGA 3'; 5' TAAGAC 3'; 5' AAGACT 3'; 5' AGACTG 3'; and 5' GACTGA 3'.

12. A kit of claim 9, further comprising a DNA sampling means and a DNA sampling reagent.

13. A kit of claim 6, which further comprises a control.

14. A kit of claim 11, wherein said detection oligonucleotide includes a label.

15. A method for treating a subject for a disease or condition, which is caused by or contributed to by an inappropriately high level of IL-1 $\beta$ , comprising the steps of:

- a) detecting an IL-1B allele (+6912) or an allele in linkage disequilibrium with an IL-1B allele (+6912) in a nucleic acid from the subject, wherein detection of IL-1B allele 2 (+6912) or an allele in linkage disequilibrium with IL-1B allele 2 (+6912) indicates that the patient has an increased susceptibility for developing a disease or condition, which is caused by or contributed to by an inappropriately high level of IL-1 $\beta$ ; and
- b) administering an IL-1 $\beta$  agonist to the subject.

16. A method of claim 15, wherein the disease or disorder is an inflammatory disease.

17. A method of claim 16, wherein said inflammatory disorder is selected from the group consisting of: coronary artery disease, osteoporosis, nephropathy in diabetes mellitus, alopecia areata, Graves disease, systemic lupus erythematosus, lichen sclerosis, ulcerative colitis, diabetic retinopathy, periodontal disease, juvenile chronic arthritis (e.g. chronic iridocyclitis), psoriasis, insulin dependent diabetes in DR 3/4 patients, asthma, chronic inflammatory liver disease, chronic inflammatory lung disease, lung fibrosis, liver fibrosis, rheumatoid arthritis and ulcerative colitis.

18. A method of claim 15, wherein the IL-1B allele (+6912) is detected by hybridizing the nucleic acid sample with at least one detection oligonucleotide that contains 6 consecutive nucleotides selected from the group consisting of: 5' ATTAAC 3'; 5' TTAACA 3'; 5' TAACAC 3'; 5' AACACT 3'; 5' ACACTG 3'; 5' CACTGA 3'; 5' ATTAAG 3'; 5' TTAAGA 3'; 5' TAAGAC 3'; 5' AAGACT 3'; 5' AGACTG 3'; and 5' GACTGA 3'.

19. A method of claim 15, wherein the IL-1B allele (+6912) is detected by contacting the sample DNA with a *HinfI* restriction enzyme and analyzing the restriction fragments, wherein a band pattern of 89, 76 and 61 base pair fragments identifies the IL-1B allele 2 and 76,61,54 and 35 bands identify the IL-1B allele 1.

20. A method for establishing an IL-1B (+6912) population profile in a specific population of individuals, comprising determining the IL-1B (+6912) genetic profile of the individuals in the population and establishing a relationship between IL-1B (+6912) genetic profiles and specific characteristics of the individuals.

21. A method of claim 20, wherein the specific characteristics of the individual include a susceptibility to developing a disease or condition, which is caused by or contributed to

by IL-1 $\beta$ .

22. A method for identifying a compound that modulates IL-1B allele 2 (+6912) expression, comprising the steps of:

- (a) contacting an appropriate amount of the compound with a cell or cellular extract, which expresses IL-1B allele 2 (+6912); and
- (b) determining the resulting IL-1B expression level, wherein an increase or decrease in the IL-1B expression level in the presence of the compound as compared to the expression in the absence of the compound indicates that the compound is a modulator of IL-1B expression.

23. A method of claim 22, wherein the compound is an agonist.

24. A method of claim 22, wherein the compound is an antagonist.

25. A method of claim 22, wherein the compound is a member selected from the group consisting of a polypeptide, a nucleic acid, a peptidomimetic, and a small molecule.

26. A method of claim 25, wherein the nucleic acid is a member selected from the group consisting of an antisense, a ribozyme, and a ~~triplex~~ nucleic acid.

27. A method of claim 22, which additionally comprises the step of preparing a pharmaceutical composition from the compound.

28. A method of claim 22, wherein said cell is contained in an animal.

29. A method of claim 28, wherein the animal is transgenic.

30. A method of claim 29, wherein the IL-1B allele 2 (+6912) gene is human.

31. A compound identified by the method of claim 22.

32. A compound of claim 31, which is selected from the group consisting of: a small molecule, a polypeptide, a nucleic acid and a peptidomimetic.

33. A compound of claim 32, wherein the nucleic acid is selected from the group

consisting of: an antisense molecule, a ribozyme and a triplex nucleic acid.

34. An isolated nucleic acid as shown in SEQ ID. No. 2.

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35. An isolated nucleic acid of claim 34, which is comprised of between about 100 and about 7000 nucleotide and contains a guanine at position 6912.

36. An isolated nucleic acid of claim 34, which is comprised of between about 5000 and about 7000 nucleotides.

37. A transgenic non-human animal which contains and expresses an isolated nucleic acid of claim 34 in at least some of its cells.

38. A transgenic non-human animal of claim 37, which is heterozygous for the isolated nucleic acid of claim 34.

39. A transgenic non-human animal of claim 37, which is homozygous for the isolated nucleic acid of claim 34.

40. A transgenic non-human animal of claim 37, which exhibits a phenotype that is characteristic of an inflammatory disorder.

41. A transgenic non-human animal of claim 40, wherein said inflammatory disorder is selected from the group consisting of: coronary artery disease, osteoporosis, nephropathy in diabetes mellitus, alopecia areata, Graves disease, systemic lupus erythematosus, lichen sclerosis, ulcerative colitis, diabetic retinopathy, periodontal disease, juvenile chronic arthritis (e.g. chronic iridocyclitis), psoriasis, insulin dependent (Type I) diabetes, asthma, chronic inflammatory liver disease, chronic inflammatory lung disease, lung fibrosis, liver fibrosis, rheumatoid arthritis and ulcerative colitis and an arteritic disorder.

42. A method for identifying an agent as being an IL-1 $\beta$  antagonist, comprising administering the agent to a transgenic non-human animal of claim 37 and observing the effect on the animal's phenotype, wherein a amelioration of a phenotype characteristic of an inflammatory disorder indicates that the agent is an IL-1 $\beta$  antagonist.

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